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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/642,970	08/18/2003	Olaf Ritzeler	DEA V2002/0063 US NP	3385
7590 09/27/2005			EXAMINER	
Julie Anne Knight Aventis Pharmaceuticals, Inc. Patent Department Route #202-206/ P.O. Box 6800 Bridgewater, NJ 08807-0800			RAO, DEEPAK R	
			ART UNIT	PAPER NUMBER
			1624	
DATE MAILED: 09/27/2005				

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/642,970

Applicant(s)

RITZELER ET AL.

Examiner

Deepak Rao

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 18 August 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-14 are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-14 are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>03012004</u> . | 6) <input type="checkbox"/> Other: _____  |

### DETAILED ACTION

Claims 1-14 are pending in this application.

#### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treatment of rheumatoid arthritis, does not reasonably provide enablement for a method of treatment or prophylaxis of all diseases associated with an increased activity of I $\kappa$ B kinase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed. The determination that “undue experimentation” would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations.

The instant claims are drawn to ‘a method for producing a pharmaceutical for the prophylaxis and therapy of a disease associated with an increased activity of I $\kappa$ B kinase’ and the specification provides that such diseases include chronic diseases of the locomotory apparatus, degenerative joint diseases, inflammatory bowel diseases, Alzheimer’s diseases, cancer, viral infections, parasitic infections, diabetes, etc. (see page 10). First, the instant claims cover ‘diseases’ that are known to exist and those that may be discovered in the future, for which there is no enablement provided. The specification provides an *in vitro* assay to determine I $\kappa$ B kinase inhibition activity (see pages 39-44) and the IC<sub>50</sub> data for some of the exemplified compounds is provided, however, there is nothing in the disclosure regarding how this *in vitro* data correlates to the treatment of the disorders intended by the instant claims. A state of the art reference, Xiao et al. (The EMBO Journal, 2001), state that “A well-characterized pathway leading to NF- $\kappa$ B activation is through phosphorylation and subsequent degradation of I $\kappa$ B $\alpha$ . This canonical NF- $\kappa$ B signaling pathway depends on a multisubunit I $\kappa$ B kinase (IKK), which responds to various stimuli, such as the inflammatory cytokine tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ), the mitogen phorbol 12-myristate 13-acetate (PMA) and certain viral proteins. .... Although the cellular signals stimulating p100 processing remain unknown, the NF- $\kappa$ B-inducing kinase (NIK) has been shown to a key regulatory role in the proteolysis event. .... The NIK-induced p100 processing involves site-specific phosphorylation and subsequent ubiquitylation of p100, although it is unclear whether NIK or a NIK-associated kinase catalyzes the p100 phosphorylation” (see page 6805).

The disorders encompassed by the instant claims include “cancer”, which has been proven to be extremely difficult to treat. Further, there is no reasonable basis for assuming that the myriad of compounds embraced by the claims will all share the same physiological

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properties since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art for assuming the same. Note *In re Surrey*, 151 USPQ 724 regarding sufficiency of disclosure for a Markush group.

Further, there is no disclosure regarding how the patient in need of such specific kinase inhibiting activity is identified and further, how all types of cancer are treated. See MPEP § 2164.03 for enablement requirements in cases directed to structure-specific arts such as the pharmaceutical art. Receptor activity is generally unpredictable and highly structure specific area, and the data provided of the single compound is insufficient for one of ordinary skill in the art in order to extrapolate to the other compounds of the claims. It is inconceivable as to how the claimed compounds can treat the extremely difficult diseases embraced by the instant claims.

A ‘cancer’ is anything that is caused by an abnormal tissue growth. That can be growth by cellular proliferation more rapidly than normal, or continued growth after the stimulus that initiated the new growth has ceased, or lack (partial or complete) of structural organization and/or coordination with surrounding tissue. It can be benign or malignant. Thus, such term covers not only all cancers, but also covers precancerous conditions such as lumps, lesions, polyps, etc. No compound has ever been found to treat cancers of all types generally. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. The existence of such a “silver bullet” is contrary to our present understanding of oncology. Cecil Textbook of Medicine states that “each specific type has unique biologic and clinical features that must be appreciated for proper diagnosis, treatment and study” (see the enclosed article, page 1004). Different types of cancers affect different organs and have different methods of growth and harm to the body. Also see *In re Buting*, 163

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USPQ 689 (CCPA 1969), wherein 'evidence involving a single compound and two types of cancer, was held insufficient to establish the utility of the claims directed to disparate types of cancers'. Thus, it is beyond the skill of oncologists today to get an agent to be effective against cancers generally.

Enablement for the scope of "treating inflammatory disorder" generally is not present. For a compound or genus to be effective against inflammation generally is contrary to medical science. Inflammation is a process, which can take place individually any part of the body. There is a vast range of forms that it can take, causes for the problem, and biochemical pathways that mediate the inflammatory reaction. There is no common mechanism by which all, or even most, inflammations arise. Mediators include bradykinin, serotonin, C3a, C5a, histamine, assorted leukotrienes and cytokines, and many, many others. Accordingly, treatments for inflammation are normally tailored to the particular type of inflammation present, as there is no, and there can be no "magic bullet" against inflammation generally. Inflammation is the reaction of vascularized tissue to local injury; it is the name given to the stereotyped ways tissues respond to noxious stimuli. These occur in two fundamentally different types. Acute inflammation is the response to recent or continuing injury. The principal features are dilatation and leaking of vessels, and recruitment of circulating neutrophils. Chronic inflammation or "late-phase inflammation" is a response to prolonged problems, orchestrated by T-helper lymphocytes. It may feature recruitment and activation of T- and B-lymphocytes, macrophages, eosinophils, and/or fibroblasts. The hallmark of chronic inflammation is infiltration of tissue with mononuclear inflammatory cells. Granulomas are seen in certain chronic inflammation situations. They are clusters of macrophages, which have stuck tightly together, typically to wall

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something off. Granulomas can form with foreign bodies such as aspirated food, toxocara, silicone injections, and splinters. Otitis media is an inflammation of the lining of the middle ear and is commonly caused by *Streptococcus pneumoniae* and *Haemophilus influenzae*. Cystitis is an inflammation of the bladder, usually caused by bacteria. Blepharitis is a chronic inflammation of the eyelids that is caused by a staphylococcus. Dacryocystitis is inflammation of the tear sac, and usually occurs after a long-term obstruction of the nasolacrimal duct and is caused by staphylococci or streptococci. Preseptal cellulitis is inflammation of the tissues around the eye, and Orbital cellulitis is an inflammatory process involving the layer of tissue that separates the eye itself from the eyelid. These life-threatening infections usually arise from staphylococcus. Hence, these types of inflammations are treated with antibiotics. Certain types of anti-inflammatory agents, such as non-steroidal anti-inflammatory medications (Ibuprofen and naproxen) along with muscle relaxants can be used in the non-bacterial cases. The above list is by no means complete, but demonstrates the extraordinary breadth of causes, mechanisms and treatment (or lack thereof) for inflammation. It establishes that it is not reasonable to any agent to be able to treat inflammation generally.

Further, neurological or neurodegenerative disorders covers diverse disorders such as Alzheimer's disease, dementia, hereditary cerebellar ataxias, paraplegias, syringomyelia, phakomatoses, and much more. In fact, Layzer, Cecil Textbook of Medicine (article enclosed), states that 'some degenerative diseases are difficult to classify because they involve multiple anatomic locations' (see page 2050). For example, Alzheimer's disease has traditionally been very difficult or impossible to prevent or even to treat effectively with chemotherapeutic agents. See e.g., the Cecil Textbook of Medicine, 20th edition (1996), Vol. 2, wherein it is stated that

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‘[t]here is no cure for Alzheimer’s disease, and no drug tried so far can alter the progress of the disease’ (pg. 1994).

There is no evidence of record, which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disease(s) or disorder(s) claimed herein and therefore, require the treatment. Next, applicant’s attention is drawn to the “Revised Utility and Written Description Guidelines, at 66 FR 1092-1099, 2001” wherein it is emphasized that ‘a claimed invention must have a specific and substantial utility’. The disclosure in the instant case is not sufficient to enable the instantly claimed ‘prophylaxis or therapy of a disease associated with an increased activity of I $\kappa$ B kinase’ solely based on the kinase inhibitory activity disclosed for the compounds.

It is inconceivable as to how the claimed single class of compounds can treat infectious diseases such as viral diseases generally. For example, there is no known common therapeutic mechanism for viral diseases generally. There are more than 400 distinct viruses that infect humans producing a wide range of diseases. The Merck Manual of Diagnosis and Therapy states that “Several hundred different viruses infect humans. Because many have been only recently recognized, their clinical effects are not fully understood” and “Only a few viral diseases can be diagnosed clinically or epidemiologically” see

<http://www.merck.com/mrkshared/mmanual/section13/chapter162/162a.jsp>. Cecil Textbook of Medicine states that “for many viral infections, no specific therapy exists. Proper use of antivirals requires specific viral diagnosis” (see the enclosed article, page 1742).

Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds. Pharmacological activity in



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general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, “the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved”. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

It is inconceivable as to how the claimed compounds can treat the entire class of viral infections, parasitic infectious diseases, involving various organisms and numerous strains thereof. See <http://www.aber.ac.uk/~mpgwww/Edu/ParProto/ProtoTxt.html> which reports that ‘there are over 50,000 species of protozoa, of which a fifth are parasitic’ and that ‘there is great variability between different strains’. Regarding *Coccidia* the article provides that “The number of different species of coccidian is staggering..... the vast majority of Coccidia species are probably yet to be described”. In reference to ‘parasitic diseases’, The Merck Veterinary Manual provides that ‘clinical experience with many of the diseases is limited’ (see <http://www.merckvetmanual.com/mvm/index.jsp?cfile=htm/bc/170709.htm>). The instant claim language encompasses all types of parasitic disorders occurring in animals including human in general. There is no evidence of record, which would enable the skilled artisan in the identification of the animal which has the potential of becoming afflicted with the disease(s) or disorder(s) claimed herein and therefore, require the treatment. Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds. For example, the state of the art regarding a known parasitic disorder, Schistosomiasis, indicates that “Control of schistosomiasis is extremely difficult” (see <http://www.anti-parasite.com/wrmsflks.html>). Also, regarding a common skin disorder that occurs in dogs, it is expressed that “Generalized demodicosis is serious and often difficult to

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treat” (see <http://pethealthclinic.tripod.com/skin/>). Therefore, the state of the art provides the need of undue experimentation for the instantly claimed therapeutic benefits.

Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, “the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved”. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

Next, applicant’s attention is drawn to the “Revised Utility and Written Description Guidelines, at 66 FR 1092-1099, 2001”, wherein it is emphasized that ‘a claimed invention must have a specific and substantial utility’. The disclosure in the instant case is not sufficient to enable the instantly claimed therapeutic effect on these assorted diseases solely based on the *in vitro* inhibitory activity disclosed for the compounds.

Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, ‘the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved’. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

The scope of the above method claims is not adequately enabled solely based on the *in vitro* I $\kappa$ B kinase inhibition activity provided in the specification. The instant claims are drawn to “a method for the **prophylaxis** and therapy of a disease ....” and therefore, the instant claim

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language embraces disorders not only for the treatment, but also for “prevention” which is not remotely enabled. The instant compounds are disclosed have proton pump inhibitory activity and it is recited that the instant compounds are useful in the “prevention” of gastrointestinal diseases for which applicants provide no competent evidence. “To prevent” actually means *to anticipate or counter in advance, to keep from happening etc.* (as per Websters II Dictionary) and therefore it is not understood how one skilled in the art can reasonably establish the basis and the type of subject to which the instant compounds can be administered in order to have the “prevention” effect. The only test example in the specification provides assay measuring the I $\kappa$ B kinase activity, however, it is inconceivable as to how the claimed compositions, not only treat but also “prevent” a myriad of diseases with different etiologies. Further, there is no evidence of record, which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disease(s) or disorder(s) claimed herein. The specification does not provide any disclosure regarding the prevention of the diverse disorders of the instant claims. For example, a neurodegenerative disease such as Alzheimer's disease has no known cause and has been treated mostly by choline esterase inhibitors to prolong the activity of acetylcholine. There is no evidence of record, which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disease(s) or disorder(s) claimed herein.

The determination that “undue experimentation” would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the above noted factual considerations. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404.

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There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is “undue.” These factors include, but are not limited to:

- (A) The breadth of the claims;
- (B) The nature of the invention;
- (C) The state of the prior art;
- (D) The level of one of ordinary skill;
- (E) The level of predictability in the art;
- (F) The amount of direction provided by the inventor;
- (G) The existence of working examples; and
- (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

**The breadth of the claims**

The breadth of the instant claims are seen to encompass methods for treating or preventing diseases associated with an increased activity of I $\kappa$ B kinase administering an I $\kappa$ B kinase inhibitor of the instant claims and is seen to include the conditions such as Alzheimer’s disease, AIDS, rheumatoid arthritis, cancer, etc.

**The nature of the invention**

Currently, there are no known agents with the chemotherapeutic efficacy to **prevent** all types of cancer, Alzheimer’s disease, AIDS, etc. The art does not disclose an active agent or combination of active agents, which are recognized to **prevent** the conditions cited supra. The

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prior art does not teach or disclose a treatment modality wherein healthy subjects are administered an active agent or agent(s) and there is evidence that none of the associated symptoms or disease state characteristics are ever manifested. The disclosure does not direct the skilled artisan to art, which satisfies the requirement for preventing a disease state associated with I $\kappa$ B inhibition.

**The state of the prior art**

There was no conclusive evidence for the prevention of any of the claimed diseases in the state of the art.

**The level of one of ordinary skill**

The level of skill is that of a MD or PhD.

**The level of predictability in the art**

Since the art does not disclose any chemotherapeutic preventive agents, the skilled artisan would not predict, in the absence of proof to the contrary, that the active agent(s) instantly claimed are efficacious in preventing the claimed inflammatory disorders. The assertion of a broad application as set forth in the instant method claims necessarily requires evidence to support applicant's asserted methods. The examiner notes there are no known pharmaceutical agents recognized as **preventive** agents for the conditions claimed, and one of skill in this art could not predict, from the evidence of record, that the active agents asserted to be useful in the instantly claimed method, can indeed prevent all types of cancer, Alzheimer's disease, AIDS, etc.

**The amount of direction provided by the inventor**

The examiner notes, there is not seen sufficient guidance provided in the form of

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administration profiles, combination ratios of the active agents or references to same in the prior art to provide the skilled artisan with sufficient guidance to practice the instant preventive method. **Prophylaxis** or **prevention** is seen to encompass administering the active agent to a baby or small child or healthy adult, and noting the fact that symptoms of the inflammatory disorders of the claims.

#### **The existence of working examples**

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). There is not seen in the disclosure, sufficient evidence to support applicant's claims of prevention. There is not seen sufficient working examples or data from references of the prior art providing a nexus between that which applicant asserts as proof of a method for preventing all types of cancer, Alzheimer's disease, AIDS, etc. or extrapolation from the data and evidence currently provided on the record to support methods drawn to preventing any condition.

#### **The quantity of experimentation needed to make or use the invention**

The diagnosis of each of the disease is generally suggested by medical history and reports of endoscopy, cytology, X-ray, biopsy, etc. depending on the symptoms, signs and complications, which is essential to establish the dosage regimen for appropriate treatment or prevention. The disclosure does not provide any guidance towards the dosage regimen required to facilitate the prevention of the claimed disorders nor indicate competent technical references in the appropriate method of preventing.

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(Only a few of the claimed diseases are discussed here to make the point of an insufficient disclosure, it does not definitely mean that the other diseases meet the enablement requirements).

Thus, factors such as “sufficient working examples”, “the level of skill in the art” and “predictability”, etc. have been demonstrated to be sufficiently lacking in the use of the invention. In view of the breadth of the claim, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

1. In claim 1, in formula (I) the acyclic nitrogen in the structural formula has an open valency. It is not clear what is intended to be substituted on the nitrogen.
2. Regarding claim 4, the phrase "such as" (see step b) renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

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3. Claim 6 recites "A method for producing a pharmaceutical ...", however, does not provide any steps involved in the preparation.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 6-14 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-2 and 6-17 of copending Application No. 10/642,974. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims substantially overlap the compounds of the reference claims. The reference claims are also drawn to a method for the treatment of pain associated with various diseases administering I $\kappa$ B inhibitors such as those of formula (I). The instant claims also recite treatment of diseases associated with I $\kappa$ B inhibitor activity. It would have been obvious to one having ordinary skill in the art at the time of the invention to select any of the species of the genus taught by the reference, including those instantly claimed, because the skilled chemist would have had the reasonable expectation that



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any of the species of the genus would have similar properties and, thus, the same use as taught for the genus as a whole. One of ordinary skill in the art would have been motivated to select the claimed compounds from the genus in the reference since such compounds would have been suggested by the reference as a whole.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Receipt is acknowledged of the Information Disclosure Statement filed on March 1, 2004 and a copy is enclosed herewith.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deepak Rao whose telephone number is (571) 272-0672. The examiner can normally be reached on Tuesday-Friday from 6:30am to 5:00pm.

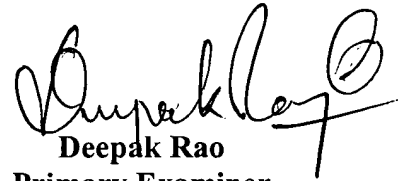
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson, Acting-SPE of 1624, can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications

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may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



**Deepak Rao**  
**Primary Examiner**  
**Art Unit 1624**

September 19, 2005